REMARKS

The first paragraph of the specification has been deleted and a replacement paragraph submitted. In the new paragraph, reference to U.S. Application Serial No. 09/062,013 has been amended to reflect issuance of the application as U.S. Patent No. 6,455,686.

Claims 25-51 have been canceled. New Claims 52-65 have been submitted.

Claim 52 is directed towards a protein produced from a recombinant vector. Specifically, the claim recites the production of a protein using a means to encode a mapB protein and a means to express the mapB protein from the encoding means. Support for mapB proteins produced in this manner can be found in the specification, for example, on page 36, lines 5-23, through page 37, lines 1-3, and on page 39, lines 20-23, through page 42, lines 1-6. The claim also specifies the protein must be able to bind an antibody produced against a specified sequence. Support for such activity can be found in the specification, for example, on page 10, lines 6-8, and on page 47, lines 10-23, through page 48, lines 1-19.

Claim 53 tracks previous Claim 27(b) with the exception Claim 53 also includes SEQ ID NO:2.

Claims 54 and 61 substantially track previous Claim 30 with the exception Claims 54 and 61 also include SEQ ID NO:2.

Claims 55 and 62 are drawn to an isolated protein consisting of a specified amino acid sequence. Support for proteins having the specified sequences can be found in the specification, for example, on page 20, lines 1-13.

Claim 56 substantially tracks previous Claim 25(a); however, the claim has been re-written to specify the sequence encoding the protein hybridize with a specified sequence.

Claim 57 tracks previous Claim 26.

Claim 58 substantially tracks previous Claim 38 with the exception the claim has been re-written to specify the protein encoding sequence comprise a specified sequence.

Claim 59 tracks previous Claim 29.

Claim 60 substantially tracks previous Claim 27; however, the new claim has been re-drafted as an independent claim and the immune response has been clarified as the ability of the protein bind an antibody raised against a protein having a specified sequence.

Claim 63 substantially tracks previous Claim 32 except the dependency has been changed.

Claim 64 substantially tracks previous Claim 33 except the dependency has been changed. Accordingly, Applicants submit no new matter has been entered into the specification.

I. Rejections Under 35 U.S.C. §112, first paragraph - enablement

The Examiner has rejected Claims 25-28 and 30-39 under 35 U.S.C.§112 for lack of enablement stating that while the specification enables proteins comprising an amino acid selected from SEQ ID NO's 1-11, 13, 15, 18 and 21, and proteins encoded by a nucleic acid molecule comprising SEQ ID NO:14, 17 or 20 and kits and compositions comprising such proteins, it does not teach how to make *any* protein as set forth in the claims.

With regard to proteins encoded by nucleic acid molecules described using hybridization conditions, the Examiner contends the specification provides insufficient guidance as to the structure associated with function with regard to proteins encoded by nucleic acid molecules of at least 150 nucleotides that hybridize to a nucleic acid molecule having the sequence of SEQ ID NO: 16, 19 or 22. The Examiner states the art is unpredictable such that determining the effect of mismatches is unpredictable and there is no guarantee the polynucleotide will encode the same protein. In addition, the Examiner contends the term "comprising" is open-ended and the specification lacks guidance as to which nucleotides can be added and whether the encoded protein maintains the same function as the protein encoded by SEQ ID NO's 16, 19 and 22. Finally, the Examiner states there is insufficient guidance as to the structure-function relationship in proteins encoded by nucleic acid molecules of at least about 15 nucleotides. According to the Examiner, because there is no nexus between structure and function, in order to practice the instant invention, one skilled in the art would have to engage in undue experimentation. The Examiner has applied the same reasoning to proteins encoded by nucleic acid molecules at least 95% identical to a specified SEQ ID NO, proteins having a 30 amino acid region identical to a 30 amino acid region form a specified SEQ ID NO and to proteins 90% identical to a specified SEQ ID NO.

Although Applicants believe proteins encoded by nucleic acid molecules of 15 nucleotides are enabled by the instant Application, in an effort to expedite prosecution of the instant Application, reference to such proteins has been removed from the newly submitted claim set. Additionally, current Claim 56, claiming a protein encoded by nucleic acid molecules having specific hybridization characteristics, has been drafted to recite the claimed protein have a

specific function, namely that the protein binds an antibody raised against a protein having the amino acid sequence of SEQ ID NO:15. Applicants believe such proteins are enabled by the instant specification. Under 35 U.S.C.§112, first paragraph, in order to satisfy the enablement requirement, the specification must teach one of skill in the art how to make and use what the inventors consider their invention. Claim 56 clearly states the conditions to be used in isolating nucleic acid molecules encoding proteins of the instant invention. Not only would one of skill of the art be capable of understanding and performing such a hybridization, but such hybridizations are also described in the specification, for example, on page 3, lines 21-23, through page 4, lines 1-5, and on page 13, lines 18-23, through page 17, lines 1-7. The hybridization conditions described in the claim determine the basic structure (i.e. sequence) of the nucleic acid molecules that will be obtained. Contrary to the Examiner's statements, nucleic acid molecules isolated using these conditions will not encode *any* protein but only a limited set of closely related proteins. In addition to specific hybridization conditions, the claim specifies the protein encoded by the hybridizing nucleic acid molecule must be able to bind an antibody raised to a protein having the amino acid sequence of SEQ ID NO:15. Assays to perform such an analysis are well know to those skilled in the art and are also taught in the specification, for example, on page 95, lines 10-23, through page 96, lines 1-20. Since the claim clearly requires the isolated protein have a particular structure (sequence) and a particular function, Applicants contend the claim couples structure with function. Applicants further contend that, using the conditions and assays outlined in the claim and taught in the specifications, one of skill in the art would be able to isolate proteins of the instant invention. Applicants acknowledge that to isolate and test molecules falling within the scope of the claims would require a fair amount of work but Applicants do not believe such work amounts to undue experimentation. Hybridization assays are standard in the art and have been in use for many years (see for Example Sambrook, *et al.*, 1989, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Labs) Similarly, ELISA assays useful in screening proteins for their ability to bind antibodies are standard in the art and well known to those skilled in the art. In addition, such assays are capable of automation meaning a large number of proteins can be screened quickly and easily. As stated by the court in *In re Wands* (CAFC) 8USPQ2d pg. 1405, "Experimentation is not precluded by some experimentation such as routine screening." The court further noted that "...a considerable amount of experimentation is permissible if it is merely routine..." (*supra*). Applicants contend

the screening of proteins required in the instant case amounts to routine screening and therefore would not constitute undue experimentation.

With regard to proteins having an amino acid sequence 90% identical to a disclosed SEQ ID NO (Claims 53 and 60), the Examiner has issued similar arguments to those described above for proteins encoded by hybridizing nucleic acid molecules. Applicants believe such proteins to be enabled for the reasons outlined above. Briefly, the structure of such proteins is clearly defined in the claims: 90% identity to a known sequence. Applicants note the proteins claimed by Claims 53 and 60 have an associated function of binding an antibody generated to a protein having the sequence of SEQ ID NO:15. While the claim does not specifically specify what type of changes should be made and where they should be made, Applicants contend such limitations are unnecessary within the claim. The types of changes to be made can be found in the specification, for example, on page 30, lines 15-19. The claim specifies such changes can be made anywhere within the protein so long as the sequence does not vary more than 10% from the disclosed SEQ ID NO's and the protein retains the specified activity. Applicants contend it is well within the ability of one skilled in the art to produce a protein having up to 10% variability from the disclosed SEQ ID NO's. Likewise, as described above, Applicants contend it is also within the ability of one skilled in the art to screen such proteins for the specified activity. As described above, such screening would be routine and would not constitute undue experimentation.

Finally with regard to proteins comprising 30 contiguous amino acids identical to 30 amino acids from disclosed SEQ ID NO's, the Examiner has stated such claims are open-ended and lack sufficient guidance for the sequence of the protein outside of the 30 amino acid region. Applicants contend the sequence outside of the 30 amino acid region is irrelevant; what is being claimed is the use of the 30 amino acid region itself. As disclosed in the specification, such regions have use in detecting IgE antibodies in subjects who have developed allergies to mite proteins. Since, as is taught in the specification, for example, on page 10, lines 1-3, an antibody epitope can be as small as 4 amino acids in length, applicants contend 30 amino acids is clearly large enough to contain an epitope with which to detect antibodies. It does not matter what sequences are outside the claimed region since the external sequences do not contribute to the function of binding antibodies. Since the specification clearly discloses the full-length sequence, Applicants contend all one would have to do is to choose any 30 amino acid region and use it to

construct a protein of the instant invention. Applicants believe this is clearly within the abilities of one of skill in the art.

II. Rejection Under 35 U.S.C.§112, first paragraph - written description

The Examiner has rejected Claims 25-28, 30-37 and 39 under 35 U.S.C. §112, for lack of written description. Specifically, the Examiner has stated that with the exception of the protein fragments comprising SEQ ID NO's 1-11, 13, and proteins comprising SEQ ID NO's 15, 18 and 21, there is inadequate written description about the structure associated with the function of: (a) all isolated proteins encoded by nucleic acid molecules of at least 150 nucleotides in length that hybridize to SEQ ID NO:16, 19 or 22; (b) proteins encoded by nucleic acid molecules 95% identical to SEQ ID NO:14, 17 or 20; (c) proteins comprising an amino acid sequence at least 90% identical to SEQ ID NO:15, 18 or 21; and (d) proteins comprising a 30 contiguous amino acid region identical in sequence to 30 amino acids from SEQ ID NO:15, 18 or 21.

Applicants respectfully disagree with the Examiner's assertions. Applicants have claimed proteins comprising an amino acid sequence having a well-defined relationship to disclosed SEQ ID NO's. With regard to proteins encoded by hybridizing nucleic acid molecules, such proteins are defined by the sequence of the nucleic acid molecule which itself, is determined by the hybridization conditions that are used. While it is true Applicants have not literally disclosed each and every possible sequence variant of such a nucleic acid, Applicants contend such extensive, literal disclosure is unnecessary. The conditions specified in the claims serve to place limits on which molecules will hybridize and which will not. Therefore, the structure of the nucleic acid molecule (and therefore the encoded protein) is defined as a function of the hybridization function given in the claims. Using this, one of skill in the art would easily envision all molecules encompassed by the claims.

With regard to proteins comprising an amino acid sequence 90% identical to the disclosed SEQ ID NO's (and proteins encoded by nucleic acid molecules 95% identical to disclosed SEQ ID NO's), Applicants contend such proteins are clearly described. The description starts with the disclosed sequence. The claims specify a certain number of amino acids (or corresponding nucleotides) can be changed, up to a specifically specified point. Applicants are not claiming any and all changes, only a certain percentage. One skilled in the art could certainly determine how many changes are permissible so that the newly altered protein

falls within the scope of the claims. With regard to such altered proteins having the specified activity, Applications contend it is not necessary to teach exactly which changes might or might not lead to a change in activity. The specification has described the desired activity and has also described how to test for such activity. Therefore, a skilled artisan could easily take the protein they have constructed based on the disclosed core sequence and test it for the disclosed activity.

With regard to proteins comprising 30 amino acids from the disclosed SEQ ID NO's, Applicants contend it is unnecessary to describe sequences falling outside of the 30 amino acid region. The functional part of the molecule has been clearly described; it is the 30 amino acid sequence. This region is all that is necessary to bind an antibody raised to the entire protein. Any sequence placed externally to the core 30 amino acid region will not effect the use of the protein in detecting antibodies since the basic functional region will still remain. While it is true that additional functions could be added through the addition of specific proteins, such additional functions are unnecessary; all that is necessary is that the protein bind antibodies which will be accomplished by the 30 amino acid region regardless of what sequences lay on its flanks.

III. Rejection Under 35 U.S.C. §102(e)

The Examiner has rejected Claims 25, 31-32 and 35 under 35 U.S.C. §102(e) as being anticipated by U.S. Patent No 5,866,788. The cited patent discloses a sequence of at least 15 nucleotides (36 nucleotides) identical to SEQ ID NO:16, 22 and 19.

Applicants note all reference to nucleic acid molecules of at least 15 nucleotides have been removed from the newly submitted claim set. The newly submitted claims are drawn to full length map B protein and closely related variants and to proteins comprising at least 30 contiguous amino acids identical in sequence to 30 contiguous amino acids from SEQ ID NO:15, SEQ ID NO:18 or SEQ ID NO:21. Since no such proteins or sequences are disclosed by the '788 patent, Applicants request withdrawal of the rejections under 35 U.S.C. §102(e).

IV. Rejections Under 35 U.S.C. 103(a)

The Examiner has rejected Claims 25, 33 and 34 under 35 U.S.C. §103(a) as being unpatentable over U.S. Pat. No. 5,866,788 in view of U.S. Pat. No. 6,060,590. U.S. Pat. No. 5,866,788 teaches an isolated chitinase protein from *Manduca sexta* (tobacco hornworm), such protein being encoded by a nucleic acid molecule comprising a fragment at least 15 nucleotides

in length identical in sequence to a fragment of SEQ ID NO:16, SEQ ID NO:19 and SEQ ID NO:22. U.S. Pat. No. 6,060,590 teaches a kit comprising a chitinase related protein (CHRP) for the detection of chitinase related protein. The Examiner has stated it would have been obvious to one of skill in the art to substitute the CHR protein in the kit taught by the '590 patent with a protein encoded by a nucleic acid molecule comprising a fragment of SEQ ID NO: 16, SEQ ID NO:19 or SEQ ID NO:22 as taught by the '788 patent.

Applicants note the newly submitted claims do not contain reference to fragments encoded by nucleic acid sequences of at least 15 nucleotides from SEQ ID NO:16, SEQ ID NO:19 or SEQ ID NO:22. The newly submitted claims are drawn to full length map B protein and closely related variants and to proteins comprising at least 30 contiguous amino acids identical in sequence to 30 contiguous amino acids from SEQ ID NO:15, SEQ ID NO:18 or SEQ ID NO:21. U.S. Pat. No. 5,866,788 only teaches a sequence of 36 nucleotides identical in sequence to a fragment of SEQ ID NO:16, SEQ ID NO:19 or SEQ ID NO:22. As such, Applicants contend there is nothing in the '788 patent that either alone in or combination with U.S. Patent 6,060,590 suggests or makes obvious the instant invention. In view of this, Applicants request withdrawal of the obviousness rejection.

V. Provisional Rejection Under the Judicially Created Doctrine of double Patenting

The Examiner has provisionally rejected Claims 25-39 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over co-pending Application No. 10/218,743. Applicants note that if co-pending Application No.10/218,743 issues as a patent having claims that are not patentably distinct from those of the instant application, Applicants will file a terminal disclaimer at that time.

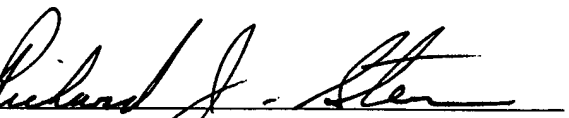
CONCLUSION

All of the submitted claims are believed to be in condition for allowance. In view of the foregoing amendments and remarks, Applicants request withdrawal of all prior rejections and issuance of the newly submitted claims.

If any questions remain regarding this Application, the Examiner is invited to contact the undersigned at (970) 493-7272 ext. 4174.

Respectfully submitted,

Dated: June 18, 2004

By: 

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